REMARKS

The Applicants thank the Office for the examination to date and for finding claims 51, 54, and 56 allowable if they are written in independent form. The Applicants respectfully request reconsideration of the present application.

Claims 45-49 and 51-56 are pending to be examined on their merits.

Claim Rejection – 35 U.S.C. § 102

Claims 45-49, 52-53, and 55 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by US 5,986,065 ("Wong"). The Applicants respectfully traverse the rejection.

Wong discloses only the prevention of thrombosis and blood clotting and does not at all teach the presently claimed methods of suppressing "hypertrophy of the vascular intima caused by tissue expression" in a patient "in need thereof," as recited in independent claims 45 and 53. At the outset, it is important to emphasize that the PTO is required to show where the prior art teaches the specific use recited in this kind of method claim. Inherency may not be used for this type of claim in light of the Federal Circuit's 2001 holding in *Rapoport v. Dement*, 254 F.3d 1053 (Fed. Cir. 2001). The *Rapoport* holding was summarized as follows in *Jansen v. Rexall Sundown*, 342 F.3d 1329 (Fed. Cir. 2003):

> A similar issue arose in *Rapoport,* an interference proceeding before the PTO's Board of Patent Appeals and Interferences. The count in that case read as follows:
>
> > A method *for treatment of sleep apneas* comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof *to a patient in need of such treatment ....*
>
> 254 F.3d at 1056 (emphases added). On appeal we gave weight to the ordinary meaning of the preamble phrase "for treatment of sleep apneas," interpreting it to refer to sleep apnea, *per se,* not just "symptoms associated with sleep apnea." *Id.* at 1059. Rapoport

> argued that the count was unpatentable on the ground that a prior art reference disclosed that a form of the compound recited in the claim could be administered, not for treatment of sleep apnea itself, but for treatment of anxiety and breathing difficulty, a symptom of apnea. *Id.* at 1061. We rejected that argument, stating, "There is no disclosure in the [prior art reference that the compound] is administered to patients suffering from sleep apnea ***with the intent to cure the underlying condition.***" *Id.* (emphasis added). Thus, the claim was interpreted to require that the method be practiced with the intent to achieve the objective stated in the preamble.

Jansen 342 F.3d 1329. (Bold emphasis added). It is clear that *Jansen* and *Rapoport* apply to the present claims.

The Office alleges that the Applicants "confusingly equate 'hypertrophy of the vascular intima' with restenosis then appear to argue that restenosis is thrombosis or undesirable blood clotting." Pages 2-3, Office Action. It appears that the PTO may have misunderstood applicants' remarks. Applicants do not equate hypertrophy of the vascular intima with restenosis. To the contrary, Applicants maintain that such hypertrophy is a **cause** (and/or phenomenon) of late stage restenosis. The Applicants respectfully submit that the PTO has misconstrued "restenosis" and "hypertrophy."

One of ordinary skill in the art understands that "restenosis" is a term referring to the narrowing of a blood vessel, regardless of whether such narrowing arises from blood clotting or tissue growth. The term "restenosis" can encompass two stages, early and late. Early restenosis usually refers to the formation of thrombus, due to a tear in plaque caused by the trauma of the angioplasty procedure itself. This tear can cause blood clots to form within the artery (thrombus) or bleeding into the wall of the artery, either of which can cause acute blockage of the artery. The teaching of **Wong** is related to prevention of the thrombus formation that occurs in this stage. In contrast, late restenosis is usually caused by the growth of new tissue at the site of the angioplasty and can be thought of as an "over exuberant" healing process. The **presently claimed methods** are directed to suppressing the hypertrophy related to formation of new tissue

in this stage. As evidenced in Hurst's The Heart by V. Fuster *et al.*, NY, McGraw-Hill, Medical Pub. Division (2004), Part I, Chapter 7, p. 148:

> "Restenosis is the development of a neointima that occurs following angioplasty, often leading to reocclusion of the initial lesion. The response of the arterial wall to the injury induced by angioplasty (removal of the endothelium and stretching of the vessel wall) involves several **distinct events**. Removal of the endothelium not only alters the paracrine hormonal environment in which VSMCs exist, but it also exposes a thrombogenic surface to which platelets and other circulating factors can adhere, resulting in the **formation of a thrombus**. In addition, injury to the underlying smooth muscle may release factors such as FGF, which have mitogenic effects on the remaining smooth muscle cells. Finally, infiltration and subsequent activation of macrophages into the denuded vessel wall bring an additional set of hormonal influences to bear on the vascular smooth muscle. The pathophysiologic consequences of these complex events include migration and **proliferation of smooth muscle cells into the intimal area, resulting in the formation of a neointima** over a period of weeks to months." (emphasis added).

Accordingly, while the teaching of Wong and the presently claimed methods are both related to "restenosis," they relate to distinct physiological conditions that occur during restenosis.

Specifically, contrary to the Office's assertion on page 3 of the Office Action, Wong's teaching indeed only relates to treating thrombosis, not "restenosis" as whole, as the latter would encompass both (i) thrombosis and (ii) hypertrophy of the intima. Furthermore, contrary to the Office's assertion, "hypertrophy," which refers to an over-proliferation of cells, as evidenced in the excerpt from Fuster *et al.* above, is distinct from the thrombus formation that is the subject of Wong's method. These two conditions are distinct from each other as proven by the afore-mentioned Fuster. Specifically, (i) thrombogenesis occurs before hypertrophy of the cells, and (ii) thrombogenesis involves blood clotting caused by platelets in the blood, not hypertrophy of the cells in the intima.

Because Wong does not teach each and every element recited in independent claims 45 and 53, it cannot anticipate claims 45 or 53 or their corresponding dependent claims.

The Office further alleges anticipation based on inherency. Page 3, Office Action. The Applicants respectfully traverse. As noted above, inherency cannot be used for the present claims in view of the Federal Circuit precedent explained above relating to "in need thereof." Thus, Applicants respectfully submit that the Office's assertion of inherency on page 3 of the Office Action is improper.

Therefore, in view of the foregoing, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

The Applicants believe that the present application is now in condition for allowance and respectfully request favorable reconsideration of the application.

The Office is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Office is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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